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14. ABSTRACT

Stimuli-responsive elastin-like polypeptides (ELPs) with controlled polymer architectures were synthesized by recombinant DNA techniques, and the structure-property relationshps and force transduction in crosslinked gels of these biopolymers were investigated as a function of their phase transition behavior. These studies provide design rules for the rational fabrication of ELP-based microactuators that function in aqueous environment to meet ONR objectives.

15. SUBJECT TERMS

Elastin-like polypeptides (ELPs); Biomimetic; Crosslinked; Biopolymers; Polymer Gels

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FINAL REPORT

GRANT #: N00014-00-1-0184

PRINCIPAL INVESTIGATOR: Ashutosh Chilkoti

INSTITUTION: Duke University

GRANT TITLE: Elastin Bioelastomers for Microactuation

AWARD PERIOD: Jan 1, 1999 - Dec 31, 2002

OBJECTIVE: To synthesize elastin-like polypeptides (ELPs) with controlled polymer architectures and to investigate the structure-property relationships and force transduction in crosslinked ELPs.

APPROACH: Genetically-encodable ELPs were be synthesized with a specified transition temperature (Tt), molecular weight, and specified type, numbers, and spatial distribution of reactive sites. Crosslinked elastomers of the ELPs were fabricated by chemical crosslinking. Kinematic parameters of actuation such as the maximum temperature-induced extensions, volumetric changes (i.e. dilatation) and intrinsic response times were quantified in free-swelling tests of crosslinked ELPs, and the mechanical properties were measured by dynamic rheology as a function of temperature.

ACCOMPLISHMENTS: Swelling experiments indicate hydrogel mass decreases by 80-90% gradually over an approximate 50°C temperature range. Strain-controlled rheology showed that gels ranged in stiffness from 0.24 to 3.7 kPa at 7°C and from 1.6 to 15 kPa at 37°C depending on protein concentration, lysine content, and molecular weight.

CONCLUSIONS: Changes in gel stiffness and loss angle with cross-linking formulation suggest a low-temperature gel structure that is nearly completely elastic, where force is transmitted almost exclusively through fully extended polypeptide chains and chemical cross-links, and a high temperature gel structure, where ELP chains are contracted and force is transmitted through chemical cross-links as well as frictional contact between polypeptide chains.

SIGNIFICANCE: Genetically-engineered ELP polymers may be chemically cross-linked through precisely spaced reactive

groups to yield thermally responsive hydrogels with "tunable" physical properties. The three parameters studied - ELP molecular weight, concentration, and lysine content - had distinct contributions to hydrogel properties that would impact the materials' performance as a microactuator, sensor, or scaffold. The degree of swelling and contraction as well as materials' stiffness and energy dissipation properties were highly sensitive to all three gel formulation parameters. Broadening of the inverse transition at high lysine content and ELP concentrations, where charge repulsion between unreacted lysine residues would be most significant, suggest that the deliberate incorporation of charged residues may be used to tune ELP porosity at high temperatures. Stiffness differences amongst formulations at the low temperature were generally amplified at the higher temperatures, demonstrating a sensitivity that could be exploited to obtain tunable mechanical properties that may be uniquely attractive for the design of bioinspired microactuators. These results suggest the potential to synthesize an array of hydrogel materials with well-defined and varied physical properties to address a wide range of design specifications for applications in microactuation and tissue engineering.

PATENT INFORMATION:

Stimuli-responsive hybrid materials containing molecular actuators and their applications. US patent submitted 2/22/00, Inventors: GP Lopez, A Chilkoti, P Atanassov, VR Goparaju.

PUBLICATIONS AND ABSTRACTS

(1) K Trabbic-Carlson, LA Setton, and A Chilkoti. Rheological and swelling characterization of chemically cross-linked hydrogels of elastin-like polypeptides, *Biomacromolecules*, **4:** 572-580 (2003).

(2) H Betre, L Setton, DE Meyer, and A Chilkoti, Genetically engineered elastin like polypeptide for cartilage repair, *Biomacromolecules*, **3:** 910-916 (2002).

(3) GV Rama Rao, S Balamurugan, DE Meyer, A Chilkoti and GP López. Hybrid bio-inorganic smart membranes that incorporate protein-based molecular switches, *Langmuir* **18:** 1819-1824 (2002).

(4) K Trabbic-Carlson, D Mishra, H Betre, L Setton and A Chilkoti. Viscoelastic behavior of chemically cross-linked hydrogels of elastin-like polypeptides, *2001 BMES Annual Fall Meeting*, October 5-7, 2001, Durham, NC.

(5) H Betre, DE Meyer, A Chilkoti and L Setton. Elastin-like polypeptide as in situ forming cartilaginous tissue scaffolds, *2001 BMES Annual Fall Meeting*, October 5-7, 2001, Durham, NC.

(6) GV Rama Rao, GP Lopez and A Chilkoti. Encapsulation of smart polymers in silica: Stimuli-responsive porous hybrid materials that incorporate molecular nano-valves, *47th Annual Meeting of the American Vacuum Society,* October, 2-6, 2000, Boston, MA.